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(088802-2454)

### REMARKS

In accordance with the present invention, there are provided nucleic acids encoding neuronal nicotinic acetylcholine receptor subunits and proteins encoded thereby. In particular, the invention relates to a family of novel mammalian neuronal nicotinic acetylcholine receptor subunits, for example, the beta2 subunit, which is a non-agonist binding subunit. Invention nucleic acids and the protein encoded thereby can be used for a variety of applications, *e.g.*, for drug design and screening. Moreover, the transformed cell lines expressing specific receptor subunits can be produced in quantity for reproducible quantitative analysis of the effects of drugs on receptor functions.

Claims 34-39 and 42 are amended and claims 45-48 are added herein to define Applicants' invention with greater particularity. These amendments and new claims do not add any new matter as they are fully supported throughout the specification and claims as originally filed.

After amending the claims as set forth above, claims 7 and 34-48 are now pending in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether a particular claim remains under examination in the application, is presented, beginning on page 2 of this paper under "Listing of Claims", with an appropriate defined status identifier.

#### I. Objections

##### A. Claim 35

Claim 35 has been rewritten in independent form pursuant to the Examiner's objection.

##### B. Claim 38

Claim 38 has been amended to depend from claim 7 pursuant to the Examiner's objection to the claim as allegedly being in improper dependent form.

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## II. 35 U.S.C. §112, First Paragraph (Written Description)

### Claims 34 and 36-44

The rejection of claims 34 and 36-44 under U.S.C. §112, first paragraph as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that Applicants had possession of the claimed invention, is respectfully traversed.

Applicants respectfully disagree with the Examiner's assertion that claims 34 and 36-44 allegedly do not comply with the written description requirement on the grounds that a large genus of polynucleotides is claimed whereas only a single species is adequately described (Office Action, page 3). Contrary to the Examiner's assertion, the specification fully satisfies the written description requirement. Thus, in addition to the sequence of beta2 presented in Figures 9A, 9B, and 9C, Applicants have previously cited examples from the specification of the biochemical and structural properties of beta2 subunits of nicotinic receptors (Response facsimile transmitted April 19, 2002). One of skill in the art would understand that the exemplary sequence of the beta2 subunit provided in the specification, in conjunction with specific functional properties provided in the specification, fully describes the claimed polynucleotides by distinguishing them from other polynucleotides encoding proteins which do not share these attributes.

While Applicants maintain that the specification adequately describes the claimed genus of polynucleotides, in the interest of expediting prosecution, claims 34, 39, and 42 have been amended herein to further define this genus as embracing those polynucleotides which exhibit *all* of the functional properties described in these claims. Each of these claims lists four functional attributes, items (i) - (iv), that, when taken together, clearly distinguish the beta2 subunit from any other subunits that comprise a neuronal nicotinic receptor. For example, attribute (i) requires that the claimed polynucleotide is unable to substitute for the gamma or delta subunits of a neuronal nicotinic acetylcholine receptor. Attribute (ii) further distinguishes the claimed polynucleotide from the alpha subunits (alpha2, alpha3, alpha4, and alpha5) which are agonist

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binding (replacement specification (mailed August 22, 2003), page 1, paragraph [0003]). Finally, attributes (iii) and (iv) cite pharmacological properties of the receptors resulting from the combination of the beta2 subunit with specific alpha subunits (replacement specification, page 18, paragraph [0100]). The *combination* of these four attributes, thus, uniquely defines this receptor subunit.

Based on the above, Applicants submit that the structural and functional description of the claimed polynucleotides fully satisfies the written description requirement. Accordingly, Applicants respectfully request reconsideration and withdrawal of this basis for rejection.

### III. 35 U.S.C. §112, First Paragraph (Enablement)

#### Claims 34 and 36-44

The rejection of claims 34 and 36-44 under 35 U.S.C. §112, first paragraph as allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the relevant art to make and/or use the invention is respectfully traversed. Contrary to the Examiner's assertion, the specification fully enables the invention.

Applicants respectfully disagree with the Examiner's assertion that the specification does not provide the guidance one of skill in the art would need to produce a functional neuronal acetylcholine receptor other than that which is presented in Figures 9A, 9B and 9C (Office Action, page 4). One of skill in the art would readily understand from the functional requirements recited in the claims, the exemplary sequence of the beta2 subunit (presented in Figures 9A, 9B and 9C), and the experimental procedures disclosed in the specification (see the replacement specification at, for example, pages 36-38) how to isolate polynucleotides which encode a beta2 subunit.

For example, claim 39 recites a "polynucleotide [that] has at least 15 contiguous bases that hybridize under high stringency conditions to the complement of the nucleotide sequence set forth in Figures 9A, 9B and 9C." One of skill in the art would recognize that only sequences that

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are closely related to the probe sequence would hybridize under high stringency conditions. An artisan could therefore obtain polynucleotide sequences which encode a beta2 subunit by performing a hybridization experiment. Methods of hybridization are well known in the art and were well known at the time the instant application was filed (see the replacement specification page 17, paragraph [0095]). In addition, guidance is provided in the specification (for example, see replacement specification at page 60, paragraph [0205]).

Once in possession of these polynucleotides, the artisan could readily test the functional properties of the proteins encoded therein. Ample guidance is provided in the specification for functional analysis (see the replacement specification at, for example, pages 48-49). The artisan would then compare the observed function with those listed in items (i) – (iv) of claim 39. Claim 39, as amended herein, cites four functional properties of beta2, *all* of which must be present in the claimed polynucleotide. As discussed above, the requirement that all four of the cited functional properties be present uniquely defines the claimed genus. Therefore, one of skill in the art would recognize that the methods described in the specification provide sufficient guidance to produce a beta2 subunit that meets the requirements set forth in items (i) – (iv) of claim 39.

Applicants submit that the enablement requirement set forth in 35 U.S.C. §112, first paragraph has been satisfied. Accordingly, Applicants respectfully request reconsideration and withdrawal of this basis for rejection.

### **III. 35 U.S.C. §112, Second Paragraph**

#### **Claims 34-44**

The rejection of claims 34-44 under 35 U.S.C. §112, second paragraph as allegedly failing to point out and distinctly claim the subject matter that Applicants regard as the invention is respectfully traversed. Applicants respectfully disagree with the Examiner's assertion that the terms "high stringency conditions," "beta2," and "alpha2, alpha3, alpha4, alpha5, beta3 or beta4"

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are vague and indefinite. Contrary to the Examiner's assertion, each of terms are well known in the art and/or are clearly described in the specification. Applicants reiterate their traversal to the basis of this rejection for at least the reasons already of record.

Briefly, with respect to claims 39-41, Applicants respectfully disagree with the Examiner's assertion that these claims are allegedly vague and indefinite for use of the phrase "under high stringency conditions" (Office Action, page 6). Contrary to the Examiner's assertion, Applicants maintain that the phrase "high stringency conditions" is well known in the art and is therefore, neither vague nor indefinite. Applicants previously cited two exemplary articles in support of this assertion (Response mailed March 15, 2004, page 9). These articles provide guidance on how to vary well known parameters in order to achieve high stringency hybridization. Thus, conditions of high stringency are well known to one of ordinary skill in the art and optimization of stringency conditions to achieve successful hybridization are within the scope of routine experimentation. Therefore, Applicants respectfully request reconsideration and withdrawal of this basis for rejection.

With respect to claims 34-44, Applicants respectfully disagree with the Examiner's assertion that these claims are allegedly vague and indefinite for use of the term "beta2" (Office Action, page 6). Contrary to the Examiner's assertion, Applicants submit that the specification provides a clear description of the beta2 subunit with reference to both structure and function. First, the amino acid sequence and the DNA sequence of an exemplary beta2 subunit are presented in Figures 9A, 9B, and 9C. Second, functional properties of the beta2 subunit are described in the specification (see the replacement specification at, for example, page 1, paragraph [0003] and page 18, paragraph [0100]). Applicants respectfully submit that the use of functional language, such as the functional properties discussed above, in combination with the structural information referred to above, to describe the term "beta2" in claims 34-44 is appropriate and in accordance with the MPEP. Section 2173.05(g), explicitly states that "functional language, does not in and of itself, render a claim improper." Therefore, contrary to the Examiner's assertion, the instant specification and the language of claims 34-44 provide a

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clear description of both structural and functional properties of beta2 which would be readily understood by one of ordinary skill. Therefore, Applicants respectfully request reconsideration and withdrawal of this basis for rejection.

With respect to claims 42-44, Applicants respectfully disagree with the Examiner's assertion that these claims are allegedly vague and indefinite for use of the terms "alpha2, alpha3, alpha4, alpha5, beta3 or beta4" allegedly rendering it impossible to determine the metes and bounds of these claims (Office Action, page 7). Contrary to the Examiner's assertion, Applicants submit that the specification discloses properties unique to each of these subunits, allowing one of skill in the art to determine the metes and bounds of these claims. For example, the structural properties of each subunit are disclosed. See, for example, Figures 18A-18C (alpha2 subunit), Figure 13 (alpha3 subunit and alpha4 subunit), Figures 28A-28C (alpha5 subunit), Figure 23 (beta3 subunit), and Figures 27A-27C (beta4 subunit). One of skill in the art could readily determine the metes and bounds of these claims (drawn to polynucleotides which encode *beta2 subunits* having specified identity with respect to the amino acid sequences of the other subunits), by determining the identity of a polynucleotide encoding a beta2 subunit with respect to any of these amino acid sequences. Therefore, Applicants respectfully request reconsideration and withdrawal of this basis for rejection.

In view of the above amendments and remarks, the present application is respectfully submitted to be in condition for allowance. Accordingly, reconsideration and favorable action with respect to the pending claims is respectfully requested. In the event any issues remain to be resolved in view of this communication, the Examiner is invited to contact the undersigned at the number given below so that a prompt disposition of this application can be achieved.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit

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Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Respectfully submitted,

Date: November 23, 2004

By 

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